

**Supplementary Table S1(A): Temporal trends in antibiotic use in infants <32 weeks' gestation without culture-confirmed sepsis, NEC and/or SIP**

|                                                  | 2012                | 2013                | 2014                | 2015                | 2016                | 2017                | 2018                | 2019                | 2020                | 2021                | 2022 <sup>a</sup>   | Total               |
|--------------------------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| <b>Number of patients</b>                        | 283                 | 276                 | 306                 | 279                 | 312                 | 286                 | 259                 | 269                 | 290                 | 275                 | 133                 | 2968                |
| <b>Inpatient days</b>                            | 17069               | 16227               | 17918               | 16115               | 17453               | 16719               | 14993               | 16600               | 16961               | 16753               | 7624                | 174429              |
| <b>Total antibiotic days</b>                     | 1332                | 1331                | 1460                | 1282                | 1218                | 1214                | 921                 | 1102                | 1064                | 1056                | 472                 | 12452               |
| <b>DOT<sup>b</sup></b>                           | 78.0                | 82.0                | 81.5                | 79.6                | 69.8                | 72.6                | 61.4                | 66.4                | 62.7                | 63.0                | 61.9                | 71.4                |
| <b>AUR (median, IQR) <sup>c</sup></b>            | 0.07<br>(0.04-0.11) | 0.07<br>(0.04-0.12) | 0.06<br>(0.04-0.11) | 0.06<br>(0.04-0.10) | 0.05<br>(0.03-0.09) | 0.05<br>(0.03-0.10) | 0.05<br>(0.03-0.08) | 0.04<br>(0.02-0.08) | 0.05<br>(0.03-0.09) | 0.04<br>(0.03-0.08) | 0.05<br>(0.03-0.10) | 0.05<br>(0.03-0.10) |
| <b>Any antibiotics (n, %)</b>                    | 274 (96.8)          | 266 (96.4)          | 295 (96.4)          | 255 (91.4)          | 272 (87.2)          | 248 (86.7)          | 227 (87.6)          | 231 (85.9)          | 259 (89.3)          | 254 (92.4)          | 121 (91.0)          | 2702 (91.0)         |
| <b>Prolonged antibiotics (n, %)<sup>d</sup></b>  | 101 (35.7)          | 93 (33.7)           | 99 (32.4)           | 66 (23.7)           | 65 (20.8)           | 76 (26.6)           | 51 (19.7)           | 60 (22.3)           | 57 (19.7)           | 53 (19.3)           | 28 (21.1)           | 749 (25.2)          |
| <b>Antibiotic days per patient (median, IQR)</b> | 3 (2-6)             | 3 (2-5)             | 3 (2-5)             | 3 (2-4)             | 2 (2-4)             | 2 (2-5)             | 2 (2-4)             | 2 (2-4)             | 2 (2-4)             | 2 (2-4)             | 2 (2-4)             | 2 (2-5)             |
| <b>Suspected EOS (n, %)</b>                      | 272 (96.1)          | 265 (96.0)          | 293 (95.8)          | 249 (89.2)          | 268 (85.9)          | 242 (84.6)          | 224 (86.5)          | 224 (83.3)          | 253 (87.2)          | 246 (89.5)          | 118 (88.7)          | 2654 (89.4)         |
| <b>Suspected LOS (n, %)</b>                      | 74 (26.1)           | 63 (22.8)           | 84 (27.5)           | 62 (22.2)           | 54 (17.3)           | 60 (21.0)           | 51 (19.7)           | 68 (25.3)           | 73 (25.2)           | 69 (25.1)           | 31 (23.3)           | 689 (23.2)          |
| <b>Mortality (n, %)</b>                          | 14 (4.9)            | 9 (3.3)             | 13 (4.2)            | 15 (5.4)            | 15 (4.8)            | 11 (3.8)            | 8 (3.1)             | 15 (5.6)            | 15 (5.2)            | 9 (3.3)             | 8 (6.0)             | 132 (4.4)           |

DOT: Days of treatment per 1000 inpatient days; AUR: antibiotic utilisation rate; IQR: interquartile range; EOS: early onset sepsis; LOS: late onset sepsis; NEC: necrotising enterocolitis.

<sup>a</sup> Represents data up to 30 June 2022; <sup>b</sup>Defined as total antibiotic days per 1000 inpatient days; DOT decreased from 2012 to 2022 (IRR 0.97, 95% CI 0.96-0.98,  $p<0.001$ ); <sup>c</sup>Defined as the number of days an infant was exposed to 1 or more antimicrobial agents divided by the total length of hospital stay; AUR decreased from 2012 to 2022 (IRR 0.98, 95% CI 0.97-0.99,  $p<0.001$ );

<sup>d</sup>Defined as antibiotic treatment  $\geq 5$  days.

**Supplementary Table S1(B): Temporal trends in antibiotic utilisation rate (AUR) in infants without culture-confirmed sepsis, NEC and/or SIP by gestational age<sup>a</sup>**

|                                  | 2012                | 2013                | 2014                | 2015                | 2016                | 2017                | 2018                | 2019                | 2020                | 2021                | <i>p</i> |
|----------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|----------|
|                                  | n=283               | n=276               | n=306               | n=279               | n=312               | n=286               | n=259               | n=269               | n=290               | n=275               |          |
| <b>Gestational age (w)</b>       |                     |                     |                     |                     |                     |                     |                     |                     |                     |                     |          |
| <b>&lt;26<br/>(n=398)</b>        | 0.13<br>(0.09-0.18) | 0.14<br>(0.09-0.19) | 0.17<br>(0.11-0.23) | 0.18<br>(0.12-0.25) | 0.15<br>(0.10-0.20) | 0.14<br>(0.09-0.18) | 0.08<br>(0.06-0.11) | 0.15<br>(0.11-0.19) | 0.15<br>(0.10-0.19) | 0.16<br>(0.11-0.21) | 0.814    |
| <b>26 to &lt;28<br/>(n=489)</b>  | 0.08<br>(0.06-0.10) | 0.07<br>(0.05-0.08) | 0.07<br>(0.05-0.08) | 0.09<br>(0.07-0.10) | 0.06<br>(0.04-0.07) | 0.06<br>(0.05-0.08) | 0.08<br>(0.06-0.10) | 0.07<br>(0.06-0.08) | 0.05<br>(0.04-0.07) | 0.06<br>(0.04-0.07) | 0.054    |
| <b>28 to &lt;32<br/>(n=1967)</b> | 0.08<br>(0.07-0.09) | 0.09<br>(0.08-0.10) | 0.08<br>(0.07-0.09) | 0.07<br>(0.06-0.08) | 0.08<br>(0.07-0.09) | 0.07<br>(0.07-0.08) | 0.06<br>(0.05-0.07) | 0.05<br>(0.04-0.06) | 0.06<br>(0.05-0.07) | 0.07<br>(0.06-0.08) | <0.001   |
| <b>All<br/>(n=2835)</b>          | 0.08<br>(0.07-0.09) | 0.09<br>(0.08-0.10) | 0.09<br>(0.08-0.10) | 0.08<br>(0.07-0.09) | 0.08<br>(0.07-0.09) | 0.08<br>(0.07-0.09) | 0.07<br>(0.06-0.07) | 0.07<br>(0.06-0.07) | 0.07<br>(0.06-0.08) | 0.07<br>(0.06-0.07) | <0.001   |

<sup>a</sup> Data presented as estimated incidence rates and 95% confidence intervals derived from negative binomial regression models adjusted for gestational age, birth weight z-score, sex and year of birth. Data for 2022 was incomplete and therefore excluded from this analysis.